Are blood groups associated with severe COVID-19 respiratory failure?

A recent study in the New England Journal of Medicine made a genome wide association analysis of 1980 patients with varying severities of COVID-19 to identify genetic factors associated with disease. The authors detected cross-replicating associations with rs11385942 at locus 3p21.31 and with rs657152 at locus 9q34.2 ($P < 5 \times 10^{-8}$). Locus 3p21.3 spans the genes SLC6A20, LZTFL1, CCR9, FYCO1, CXCR6 and XCR1 and locus 9q34.2 coincided with the ABO blood group locus; showing that blood group A was 1.45 times associated with severe COVID-19 and blood group O was almost half as likely to be associated. The authors conclude: “Our genetic data confirm that blood group O is associated with a risk of acquiring Covid-19 that was lower than that in non-O blood groups, whereas blood group A was associated with a higher risk than non-A blood groups”. The authors also found that there was no association between HLA alleles and Covid-19 severity.

Timeline of Rapid Covid-19 Genomewide Association Study (GWAS). The main events and milestones of the study are summarized in the plot. Samples from patients in
three Italian hospitals (hospital A: Fondazione IRCCS Ca’ Granda Ospedale Maggiore Policlinico, Milan; hospital B: Humanitas Clinical and Research Center, IRCCS, Milan; and hospital C: UNIMIB School of Medicine, San Gerardo Hospital, Monza) and four Spanish hospitals (hospital A: Hospital Clinic and IDIBAPS, Barcelona; hospital B: Hospital Universitario Vall d’Hebron, Barcelona; hospital C: Hospital Universitario Ramón y Cajal, Madrid; and hospital D: Donostia University Hospital, San Sebastian) were obtained around the peak of the local epidemics, and ethics applications were quickly obtained by means of fast-track procedures (i.e., every local ethics review board supported studies of coronavirus disease 2019 [Covid-19] studies by providing rapid turn-around times, thus facilitating this fast de novo data generation). All the obtained blood samples were centrally isolated, genotyped, and analyzed within 8 weeks. Control data were obtained from control participants and from historical control data in Italy and Spain. The rapid workflow from patients to target identification shows the usefulness of GWAS, a standardized research tool that often relies on international and interdisciplinary cooperation. One center alone could not have completed this study, not to mention the increase in statistical power that was available because of the contribution of patients from multiple centers. The speed of data production depended heavily on laboratory automation, and the speed of analyses reflects existing analytic pipelines and the support of public so-called imputation servers (here, the Michigan imputation server of the G. Abecasis group). QC denotes quality control.


Summary by Clive Gray